said lipidized antibody is capable of transvascular transport, enhanced organ uptake and [or] intracellular localization.

REMARKS

Applicants wish to thank Examiner Schwadron and Examiner Chan for the telephonic interview held on January 12, 2000. During this telephonic interview, a number of issues were clarified and a number of amendments were proposed which have helped Applicants to more fully address the concerns of the Examiner. Applicants thank the Examiners for their time.

In order to expedite prosecution of the present case, claims 1, 9, 14, 19 and 20 have been amended more specifically to recite that the lipidized protein (claims 1 and 14) or the lipidized antibody (claims 9, 19 and 20) is capable of transvascular transport, enhanced organ uptake and intracellular localization. Support for this amendment can be found throughout the specification and, in particular, at page 1, lines 10-13, page 5, lines 26-30, *etc.* Accordingly, no new matter has been introduced by this amendment.

As requested by the Examiner, the Applicants have reviewed the status of all U.S. patent applications disclosed in the specification. Based on this review, it is the Applicants' understanding that the status of such U.S. patent applications has not changed and, thus, no updating is required.

Claims 1-22 are pending in the above-referenced patent application; claims 1-22 are currently under examination. Claims 14-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 4-12, 24, 29-33 of copending Application Serial No. 08/483,944. Claims 1-22 are rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking adequate written description. Claims 19 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Claims 1-22 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Kabanov *et al.* (pages 33-36) or Kabanov *et al.* (pages 63-67) in view of Bischofberger *et al.* and Rodwell *et al.* Claims 1-22 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Horan *et al.*

OBVIOUSNESS-TYPE DOUBLE-PATENTING REJECTION:

Claims 14-23 are provisionally rejected under the judicially created doctrine of obviousness-type double-patenting as being unpatentable over claims 1, 2, 4-12, 24, 29-33 of copending U.S. Patent Application Serial No. 08/483,944. The Examiner has indicated that this provisional rejection can be overcome by timely filing a Terminal Disclaimer.

Applicant acknowledges that copending U.S. Patent Application Serial No. 08/483,944 has claims that are similar to those in the present case. However, Applicant is entitled to at least one patent relating to the claimed invention and, thus, upon withdrawal of the other outstanding rejections/objections in the present case, Applicant will cancel the conflicting claims in copending U.S. Patent Application Serial No. 08/483,944 or, alternatively, will file a Terminal Disclaimer. As such, Applicant respectfully requests that this provisional rejection be held in abeyance until the other outstanding objections/rejections have been withdrawn.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH:

Claims 1-22 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Examiner has alleged that there is no support in the specification as originally filed for the recitation of "organ uptake" in the proposed claims. In order to expedite prosecution of the present case, Applicant has amended claims 1, 9, 14, 19 and 20 to specifically set forth "enhanced organ uptake". In view of this amendment, the Examiner's rejection is rendered moot.

Furthermore, the Examiner has alleged that there is not support in the specification as originally filed for the recitation of "or" in claims 9, 14, 19 and 20. In order to expedite prosecution of the present case, Applicant has amended claims 9, 14, 19 and 20 to overcome the Examiner's rejection by specifically reciting "and". In view of this amendment, the Examiner's rejection is rendered moot.

Accordingly, Applicant urges the Examiner to withdraw this rejection under 35 U.S.C. § 112, first paragraph.

REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH:

Claim 19 is rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. To overcome this rejection, Applicant has corrected the typographic mistake noted by the Examiner in claim 19. Accordingly, Applicant urges the Examiner to withdraw this portion of the rejection under 35 U.S.C. § 112, second paragraph.

REJECTION UNDER 35 U.S.C. § 103(a):

Claims 1-22 remain rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Kabanov *et al.* (pages 33-36) or Kabanov *et al.* (pages 63-67) in view of Bischofberger *et al.* and Rodwell *et al.* As amended, all of the pending claims are directed to a lipidized protein (*e.g.*, a lipidized antibody) that is (1) a protein (e.g., an antibody) covalently linked to a lipid through a carbohydrate moiety; and (2) a lipidized protein (*e.g.*, a lipidized antibody) that is capable of transvascular transport, enhanced organ uptake and intracellular localization. For the reasons set forth herein, the presently claimed lipidized proteins are not obvious over the prior art.

Kabanov *et al.* is cited by the Examiner as disclosing lipidized antibodies and that such antibodies can "translocate across lipid membranes and penetrate intact cells". During the telephonic interview, it was agreed that Kabanov *et al.* does not teach lipidized proteins that comprise a polypeptide covalently attached to a lipid through a carbohydrate moiety. As such, it was agreed that the lipidized antibodies of Kabanov *et al.* are structurally different from the claimed lipidized proteins, because they are not "lipidized protein (or antibody), wherein said lipidized protein (or antibody) is a protein (or antibody) covalently linked to a lipid through a carbohydrate moiety" as is required by all the pending claims.

Rodwell *et al.* is cited by the Examiner as disclosing that an amine containing compound (such as an aspartic acid, a glutamic acid or a lysine) can be attached to antibodies by oxidation of antibody saccharides to aldehydes which can react with the amine containing

compounds. Rodwell *et al.* does not teach attaching aminolipids to antibodies. The Examiner also cites Bischofberger *et al.* as disclosing that an aminolipid can be used to attach a lipid to an immunoconjugate. Bischofberger *et al.* does not teach attaching an aminolipid to an antibody.

The teachings of Kabanov *et al.* cannot be looked out in combination with Rodwell *et al.* or Bischofberger *et al.* alone. Instead, the Federal Circuit in Dow Chemical Co., 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988) stated:

> In determining whether such as suggestion [of obviousness] can be fairly gleaned from the prior art, ***the full field of the invention must be considered***: for the person of ordinary skill is charged with knowledge of the entire body of technological literature, ***including that which might lead away from the claimed invention***.... Evidence that supports, rather than negates, patentability must be fairly considered.

5 U.S.P.Q.2d at 1531-1532 (citations omitted; emphasis added). Moreover, the Federal Circuit in Akzo N.V. v. International Trade Commission, 808 F.2d 1471, 1 U.S.P.Q.2d 1241 (Fed. Cir. 1986) stated:

> [P]rior art references before the tribunal must be read as a whole and *consideration must be given where the references diverge and teach away from the claimed invention*. Moreover, appellants cannot **pick** and **choose** among individual parts of assorted prior art references 'as a mosaic to recreate a facsimile of the claimed invention.'

Id. at 1481; 1 U.S.P.Q.2d 1241, 1246 (citations omitted). *See, In re* Mercier, 185 U.S.P.Q. 774, 778 (CCPA 1975); Ex Parte Finckle, 111 U.S.P.Q. 247, 249 (Bd. App.1956). As such, the teachings of Kabanov *et al.* must be looked out in combination with the teachings of Rodwell *et al.* and Bischofberger *et al.* as well as Horan *et al.* As explained herein, in doing so, it is seen that the references when read "as a whole", actually teach away from the claimed invention.

During the telephonic interview with Examiner Schwadron and Examiner Chan, the teachings of Horan *et al.* were discussed and it was agreed that Horan *et al.* teaches a screening method to produce lipidized molecules that are retained in the membrane as opposed to not being retained in the membrane and dissociating from the membrane, not as opposed to

crossing the membrane and localizing intracellularly. The Examiner states that the teachings of Horan *et al.* do not negate the teachings of Kabanov *et al.* The Applicant respectfully disagrees and believes that Kabanov *et al.* in combination with Horan *et al.* teach away from the present invention. The lipidized antibodies of Horan *et al.* are structurally different from the lipidized antibodies of Kabanov *et al.* The lipidized antibodies of Kabanov *et al.* localize intracellularly, while the lipidized antibodies of Horan *et al.* lodge in the membrane. It would have been apparent to one of skill in the art that the structure of the lipidized antibody is critical to its cellular localization and that the cellular localization is *a priori* unpredictable for a given lipidized antibody. One of skill in the art wishing to localize intracellularly an antibody would therefore have had no motivation to lipidize the antibody in a way different from that of Kabanov *et al.* Furthermore, there would have been no reasonable expectation of success in covalently attaching a lipid to an antibody in order to localize the lipidized antibody intracellularly.

In view of the foregoing, Applicants respectfully submit that the claimed invention is not taught in the prior art. Instead, the prior art teaches away from the claimed invention. In view of these teachings, the present invention is clearly non-obvious and, thus, patentable. Accordingly, Applicant urges the Examiner to withdraw this rejection under 35 U.S.C. § 103.

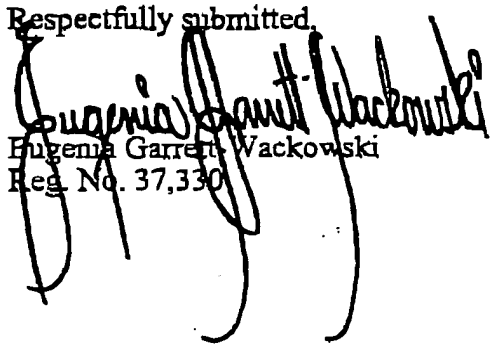
REJECTION UNDER 35 U.S.C. § 102(e):

Claims 14, 15, 19 and 20 remain rejected under 35 U.S.C. § 102(e) as being anticipated by Horan *et al.* (U.S. Patent 5,665,328). The Examiner has alleged that Horan *et al.* teaches lipidized antibodies and that it is an inherent property of antibodies to bind cells and, as all cells are part of some organ, said antibodies are capable of organ uptake. In order to expedite prosecution of the present case, claims 14, 19 and 20 have been amended to more specifically set forth Applicant's invention. In view of this amendment, the Examiner's rejection is rendered moot. Accordingly, Applicant urges the Examiner to withdraw this rejection under 35 U.S.C. § 102(e).

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is urged. If the Examiner believes a telephone conference would aid in the prosecution of this case in any way, please call the undersigned at 415-576-0200.

Respectfully submitted,



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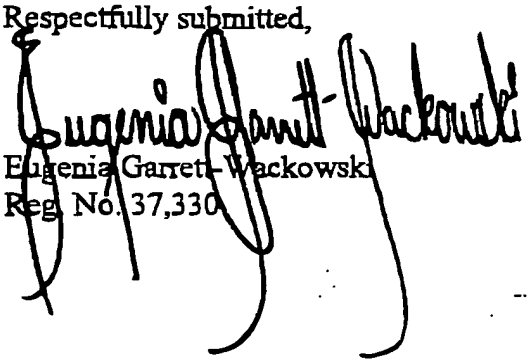
2. ☒ Please charge the filing fee of $150 for this Appeal to Deposit Account No. 20-1430 of the Undersigned. Please charge any additional fees due in connection with this paper, or credit any overpayment, to this Deposit Account. This Notice is submitted in triplicate.

Respectfully submitted,



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